

PATIENT INFORMATION LEAFLET

TYSABRI®

(natalizumab)



300 mg concentrate for solution for infusion
natalizumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

In addition to this leaflet you will be given a Patient Alert Card, which contains important safety information that you need to know before you are given TYSABRI (pronounced tie-SA-bree) and during treatment with TYSABRI.

- Keep this leaflet and the Patient Alert Card. You may need to read them again. Keep the leaflet and Alert Card with you during treatment and for six months after the last dose of TYSABRI, since side effects may occur even after you have stopped treatment.
- If you have any further questions, ask your doctor.
- If you get any side effects talk to your doctor. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:

1. What TYSABRI is and what it is used for
2. What you need to know before you use TYSABRI
3. How to use TYSABRI
4. Possible side effects
5. How to store TYSABRI
6. Contents of the pack and other information

1. What TYSABRI is and what it is used for

TYSABRI is used to treat multiple sclerosis (MS). MS causes inflammation in the brain that damages the nerve cells. TYSABRI stops the cells that cause inflammation from going into your brain. This reduces nerve damage caused by MS.

TYSABRI contains the active substance (natalizumab). This active ingredient is called a monoclonal antibody. These antibodies work by binding to proteins in the body so that the harmful effect of that protein is removed.

What are the symptoms of multiple sclerosis?

The symptoms of MS vary from patient to patient, and you may experience some or none of them.

Symptoms can include: walking problems, numbness in the face, arms or legs, problems seeing things, tiredness, feeling off-balance or light headed, bladder and bowel problems, difficulty in thinking and concentrating, depression, acute or chronic pain, sexual problems, and stiffness and muscle spasms. When the symptoms flare up, it is called a relapse (also known as an exacerbation or an attack). When a relapse occurs, you may notice the symptoms suddenly, within a few hours, or slowly progressing over several days. Your symptoms will then usually improve gradually (this is called a remission).

In clinical trials, TYSABRI approximately halved the progression of the disabling effects of MS and also decreased the number of MS attacks by about two-thirds. When you receive TYSABRI you might not notice any improvement, but TYSABRI may still be working to prevent your MS becoming worse.

NOTICE : INFORMATION DU PATIENT

2. What you need to know before you use TYSABRI

Before you start treatment with TYSABRI, it is important that you and your doctor have discussed the benefits you would expect to receive from this treatment and the risks that are associated with it.

Do not use TYSABRI

- If you are allergic to natalizumab or any of the other ingredients of this medicine (listed in section 6).
- If your doctor has told you that you have PML (progressive multifocal leukoencephalopathy). PML is a rare infection of the brain.
- If your doctor tells you that you have a serious problem with your immune system (due to disease for example, HIV or due to a medicine you are taking or have previously taken, e.g. mitoxantrone or cyclophosphamide).
- If you are taking either beta-interferon or glatiramer acetate. These medicines are for MS and cannot be used with TYSABRI (see Using other medicines, below).
- If you have an active cancer (unless it is a type of skin cancer called basal cell carcinoma).
- If you are under 18 years of age.

Warnings and Precautions

Talk to your doctor before using TYSABRI.

Infections

There have been cases of a rare brain infection called PML (progressive multifocal leukoencephalopathy) that have occurred in patients who have been given TYSABRI. PML may lead to severe disability or death.

- The symptoms of PML may be similar to an MS relapse (e.g. weakness or visual changes). Therefore, if you believe your MS is getting worse or if you notice any new symptoms, it is very important that you speak to your doctor as soon as possible.
- Speak with your partner or caregivers and inform them about your treatment. Symptoms might arise that you might not become aware of by yourself, such as changes in mood or behaviour, memory lapses, speech and communication difficulties, which your doctor may need to investigate further to rule out PML.
- You will also find this information in the Patient Alert Card you have been given by your doctor. It is important that you keep this Alert Card and show it to your partner or caregivers.

PML is associated with an uncontrolled increase of the JC virus in the brain, although the reason for this increase in some patients treated with TYSABRI is unknown. JC virus is a common virus which infects many people but does not normally cause noticeable illness.

Your doctor may test your blood to check if you have antibodies to the JC virus before you start treatment with TYSABRI. These antibodies are a sign that you have been infected by JC virus.

The risk of PML with TYSABRI is higher:

- If you have antibodies to the JC virus in your blood.
- The risk of PML is higher in patients who have antibodies to the JC virus compared to patients who do not have antibodies to the JC virus.
 - If you do not have antibodies to the JC virus, then your doctor may repeat the test regularly to check if anything has changed.
- The longer that you are on treatment especially if you have been on treatment for more than two years. It is not known if the chance of getting PML continues to rise, remains the same, or falls after you have been on TYSABRI for more than four years.
- If you have previously taken a medicine called an immunosuppressant. These medicines reduce the activity of your body's immune system.

If you have all three risks described above your chance of getting PML is higher. You should discuss with your doctor if TYSABRI is the most suitable treatment for you before you start taking TYSABRI and when you have been taking TYSABRI for more than two years.

In patients with PML a reaction known as IRIS (Immune Reconstitution Inflammatory Syndrome) is likely to occur after treatment for PML, as TYSABRI is removed from your body. IRIS may lead to your condition getting worse, including worsening of brain function.

Allergic reactions

A few patients have had an allergic reaction to TYSABRI. Your doctor will check for allergic reactions during the infusion and for 1 hour afterwards.

Will TYSABRI always work?

In a few patients who use TYSABRI, over time the body's natural defence may stop TYSABRI from working properly (the body develops antibodies to TYSABRI). Your doctor can decide whether TYSABRI is not working properly for you by testing your blood and will stop TYSABRI, if necessary.

Other medicines and TYSABRI

Tell your doctor if you are taking or have recently taken or might take any other medicines.

- You must not use TYSABRI if you are being treated with other medicines to treat your MS, such as beta-interferons or glatiramer acetate.
- You may not be able to use TYSABRI if you are currently receiving or have previously received medicines that affect your immune system, e.g. mitoxantrone or cyclophosphamide.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine

- Do not use TYSABRI if you are pregnant unless you have discussed this with your doctor. Be sure to tell your doctor immediately if you are pregnant, think you may be pregnant, or if you are planning to become pregnant.
- Do not breast-feed whilst using TYSABRI. You should discuss with your doctor whether you choose to breast-feed or to use TYSABRI.

Driving and using machines

There are no studies on the effects of TYSABRI on the ability to drive and use machines. However, if you experience dizziness, a common side effect, then you should not drive or use machines.

TYSABRI contains

Sodium phosphate, monobasic, monohydrate Sodium phosphate, dibasic, heptahydrate Sodium chloride Polysorbate 80 (E433). Water for injections.

After dilution for use, this medicinal product contains 17.7 mmol (or 406 mg) sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

3. How to use TYSABRI

TYSABRI will be given to you by a doctor experienced in the treatment of MS. Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

- The recommended adult dose is 300 mg given once every 4 weeks.

- TYSABRI must be diluted before it is given to you. It is given as a drip into a vein (by intravenous infusion), usually in your arm. This takes about 1 hour.
- Information for medical or healthcare professionals on how to prepare and administer TYSABRI is provided at the end of this leaflet.

- It is important to continue with your medicine for as long as you and your doctor decide that it is helping you. Continuous dosing with TYSABRI is important, especially during the first few months of treatment. This is because patients who received one or two doses of TYSABRI and then had a gap in treatment of three months or more, were more likely to have an allergic reaction when resuming treatment.

If you miss your dose of TYSABRI

If you miss your usual dose of TYSABRI, arrange with your doctor to receive it as soon as you can. You can then continue to receive your dose of TYSABRI every 4 weeks.

Always use this medicine exactly as described in this leaflet or as your doctor has told you. Check with your doctor if you are not sure.

If you have any further questions on TYSABRI, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet.

Serious infections may occur with TYSABRI. The symptoms of infections include:

- An unexplained fever
- Severe diarrhoea
- Shortness of breath
- Prolonged dizziness
- Headache
- Stiff neck
- Weight loss
- Lethargy

Speak to your doctor or nurse immediately if you notice any of the following:

Signs of allergy to TYSABRI, during or shortly after your infusion:

- Itchy rash (hives)
- Swelling of your face, lips or tongue
- Difficulty breathing
- Chest pain or discomfort
- Increase or decrease in your blood pressure (your doctor or nurse will notice this if they are monitoring your blood pressure).

Signs of a possible liver problem:

- Yellowing of your skin or the whites of your eyes
- Unusual darkening of the urine.

TYSABRI can also have other side effects.

Side effects are listed below by how commonly they have been reported in clinical trials:

Common side effects that may affect up to 1 in 10 people:

- Urinary tract infection
- Sore throat and runny or blocked up nose
- Shivering
- Itchy rash (hives)
- Headache
- Dizziness
- Feeling sick (nausea)
- Being sick (vomiting)
- Joint pain
- Fever
- Tiredness

Uncommon side effects that may affect up to 1 in 100 people:

- Severe allergy (hypersensitivity)
- Progressive multifocal leukoencephalopathy (PML).

Rare side effects that may affect up to 1 in 1,000 people:

- Unusual infections (so-called 'Opportunistic infections').

Speak to your doctor as soon as possible if you think you have an infection. Show the Alert Card and this package leaflet to any doctor involved with your treatment, not only to your neurologist.

You will also find this information in the Patient Alert Card you have been given by your doctor.

5. How to store TYSABRI

Keep this medicine out of the sight and reach of children.

Unopened vial:

Store in a refrigerator (2°C to 8°C).

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Do not use this medicine after the expiry date stated on the label and carton. The expiry date refers to the last day of that month.

Diluted solution:

After dilution, immediate use is recommended. If not used immediately, the diluted solution must be stored at 2°C - 8°C and infused within 8 hours of dilution.

Do not use this medicine if you notice particles in the liquid and/or the liquid in the vial is discoloured.

6. Contents of the pack and other information

What TYSABRI contains

The active substance is natalizumab. Each 15 ml vial of concentrate contains 300 mg natalizumab (20 mg/ml).

The other ingredients are: Sodium phosphate, monobasic, monohydrate, Sodium phosphate, dibasic, heptahydrate, Sodium chloride, Polysorbate 80 (E433) Water for injections.

What TYSABRI looks like and contents of the pack

TYSABRI is a clear, colourless to slightly cloudy liquid. Each carton contains one glass vial.

Marketing Authorisation Holder

Biogen Idec Limited
Innovation House
70 Norden Road
Maddenhead
Berkshire
SL6 4AY

United Kingdom Royaume-Uni

Manufacture

Biogen Idec Denmark Manufacturing ApS

Biogen Idec Allé 1

DK-3400 Hillerød

Denmark

For any further information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder Biologix, FzCo, Dubai Free Zone, Road WB 21, warehouse C17 PO Box 54405 Al Tawar Building, United Arab Emirates. Tel: (971) 4 299 7171.

This leaflet was last revised in 09/2013.

Detailed information on this medicine is available on the European Medicines Agency (EMA) web site: <http://www.ema.europa.eu>

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

Biologix FZ Co, Dubai Free Zone, Road WB 21, Warehouse C17, PO Box 54405, Al Tawar Building, United Arab Emirates.

Tel: 00971 4 2997171

Email: Pharmacovigilance@blg.net

To report any side effect(s):

- Saudi Arabia:

National Pharmacovigilance Center (NPC)

Fax: +966112057622

Call NPC at +966-11-2038222. Exts: 2317-2356-2353-2354-2334-2340

Toll free phone: 8002490000

E-mail: npc.drug@fda.gov.sa

Website: www.fda.gov.sa/npc

- UAE Ministry of Health

Registration and Drug Control Department

o Tel: 02 6117 389/029/091/318

o Fax: 02 6313742

o P.O. Box: 848 Abu Dhabi

o Email: pv@mh.gov.ae

o Website: www.cpd-pharma.ae

- Other GCC States:

Please contact the relevant competent authority

This is a Medication

- A medication is a product which affects your health, and its consumption contrary to instructions is dangerous for you.

- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medication.

- The doctor and the pharmacist are experts in medicine, its benefits and risks.

- Do not, by yourself, interrupt the period of treatment prescribed for you.

- Do not repeat the same prescription without consulting your doctor.

- Keep all medications out of reach of children.

Council of Arab Health Ministers
Union of Arab Pharmacists

The following information is intended for healthcare professionals only:

- Inspect the TYSABRI vial for particles prior to dilution and administration. If particles are observed and/or the liquid in the vial is not colourless, clear to slightly opalescent, the vial must not be used.
- Use aseptic technique when preparing TYSABRI solution for intravenous (IV) infusion. Remove flip-top from the vial. Insert the syringe needle into the vial through the centre of the rubber stopper and remove 15 ml concentrate for solution for infusion.
- Add the 15 ml concentrate for solution for infusion to 100 ml sodium chloride 9 mg/ml (0.9%) solution for injection. Gently invert the TYSABRI solution to mix completely. Do not shake.
- TYSABRI must not be mixed with other medicinal products or diluents.
- Visually inspect the diluted medicinal product for particles or discoloration prior to administration. Do not use if it is discoloured or if foreign particles are seen.
- The diluted medicinal product is to be used as soon as possible and within 8 hours of dilution. If the diluted medicinal product is stored at 2°C - 8°C (do not freeze), allow the solution to warm to room temperature prior to infusion.
- The diluted solution is to be infused intravenously over 1 hour at a rate of approximately 2 ml/minute.
- After the infusion is complete, flush the intravenous line with sodium chloride 9 mg/ml (0.9%) solution for injection.
- Each vial is for single-use only.
- Any unused medicinal product or waste material must be disposed of in accordance with local requirements.